

AMENDMENTS TO THE CLAIMS

The complete listing of all claims will serve to replace all prior versions of the claims. Applicants respectfully request favorable consideration of the present application in light of the present remarks.

Listing of claims

1. (Previously presented) A MRI detectable species according to formula (I) which upon contact with the cells or cell surfaces of a human or other animal is incorporated into or onto the animal's cells or cell surfaces and which provides contrast sufficient to clearly distinguish between normal, healthy cells and tumor cells, wherein;



D is a MRI detectable moiety selected from the group consisting of coated ferromagnetic particles, coated superparamagnetic particles and chelated complexes of paramagnetic metal ions;

S is a spacer;

N is a molecule of a nutrient or pseudo-nutrient selected from alanine, phenylalanine, arginine, putrescine, spermidine, spermine, asparagine, agmatine and glutamine and n is 0 or an integer of 1 to 5, m is an integer of 1 to 5 and p is an integer of 1 to 10, wherein when n is an integer, p = 1, m ≥ 1 and n ≤ m.

2. (Original) The MRI detectable species of claim 1 wherein D contains at least one site for attachment to the spacer S or the nutrient/pseudo-nutrient molecule N.
3. (Previously presented) The MRI detectable species of claim 1, wherein the moiety D is a chelated complex of a paramagnetic metal ion selected from the ions of transition and lanthanide metals with a chelating ligand L.
4. (Previously presented) The MRI detectable species of claim 3, wherein the paramagnetic metal ion is selected from the ions having atomic number of 21 to 29, 42,

43, 44, or 57 to 71, and the chelating ligand L is selected from the group consisting of the residue of a polyaminopolycarboxylic acid, either linear or cyclic, in racemic or optically active form, selected from the group consisting of ethylenediaminetetraacetic acid (EDTA), diethylenetriaminopentaacetic acid (DTPA), N-[2-[bis(carboxymethyl)-amino]-3-(4-ethoxyphenyl)propyl]-N-[2-[bis(carboxymethyl)amino]ethyl]-L-glycine (EOB-DTPA), N,N-bis[2-[bis(carboxymethyl)amino]ethyl]-L-glutamic acid (DTPA-GLU), N,N-Bis[2-[bis(carboxymethyl)amino]ethyl]-L- γ -glutamyl-L-glutamine, N,N-bis[2-[bis(carboxymethyl)amino]ethyl]-L-lysine (DTPA-LYS), the DTPA mono- or bis-amide derivatives, such as N,N-bis[2-[carboxymethyl][(methylcarbamoyl)-methyl]amino]ethyl] glycine (DTPA-BMA), 4-carboxy-5,8,11-tris(carboxymethyl)-1-phenyl-2-oxa-5,8,11-triazatridecan-13-oic acid (BOPTA), 1,4,7,10-tetraazacyclo-dodecan-1,4,7,10-tetraacetic acid (DOTA), 1,4,7,10-tetraazacyclododecan-1,4,7-triacetic acid (DO3A), 10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecan-1,4,7,10-tetraacetic acid (HPDO3A), 2-methyl-1,4,7,10-tetraazacyclododecan-1,4,7,10-tetraacetic acid (MCTA), ($\alpha,\alpha',\alpha'',\alpha'''$)-tetramethyl-1,4,7,10-tetraazacyclododecan-1,4,7,10-tetraacetic acid (DOTMA), 3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triacetic acid (PCTA), [4-(1,6,10-triazaundecan)-phenyl-aminocarbonylmethyl]-1,4,7,10-tetraazacyclododecan-4,7,10-triacetic acid; a derivative thereof wherein one or more of the carboxylic groups are in the form of the corresponding salts, esters, or amides; and the residue of a corresponding compound wherein one or more of the carboxylic groups is replaced by a phosphonic and/or phosphinic group selected from the group consisting of 4-carboxy-5,11-bis(carboxy-methyl)-1-phenyl-12-[(phenylmethoxy)methyl]-8-(phosphonomethyl)-2-oxa-5,8,11-triazatridecan-13-oic acid, N,N'-[(phosphonomethylimino)di-2,1-ethanediyl]bis[N-(carboxymethyl)glycine], N,N'-[(phosphonomethylimino)di-2,1-ethanediyl]bis[N-(phosphonomethyl)glycine], N,N'-[(phosphinomethylimino)di-2,1-ethanediyl]bis[N-(carboxymethyl)glycine], 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis[methylen(methylphosphonic)]acid, and 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis[methylen(methylphosphinic)]acid.

5. (Previously presented) The MRI detectable species of claim 3 wherein the complex is formed with a metal ion selected from the group consisting of Mn, Fe, Eu, Gd and Dy.
6. (Cancelled)

7. (Previously presented) The MRI detectable species of claim 1 wherein the spacer S, if present, is a homo- or hetero-bifunctional linker where the two reactive moieties are separated by alkylidene, alkenylidene, alkynylidene, cycloalkylidene arylidene, or aralkylidene radical that is optionally substituted and is optionally interrupted by heteroatoms.

8. (Previously presented) The MRI detectable species of claim 7, wherein the reactive moieties are separated by an aliphatic, straight or branched chain, that optionally is interrupted by -O-, -S-, -CO-, -NR-, -CS- groups or by aromatic rings, and optionally bear an -OR, -SR, -NRR₁, -COOR, -CONRR₁ wherein R and R₁ are hydrogen atoms.

9. (Previously presented) A process for the preparation of the MRI detectable species of claim 1, said process comprising:

- either conjugating the spacer S, if present, with the nutrient or pseudo-nutrient molecule N and combining the obtained conjugate product and the MRI detectable moiety D; or
- conjugating the MRI detectable moiety D with the spacer S, if present, and combining the obtained conjugated product with the nutrient or pseudo-nutrient molecule N.

Claims 10-12 (Cancelled)

13. (Previously presented) A pharmaceutical composition comprising a MRI detectable species of any one of claims 1 to 5 in an amount sufficient to give the desired level of contrast and at least one pharmaceutically acceptable carrier.

Claims 14-16 (Cancelled)

17. (Previously presented) A method of imaging organs, tissues, or combinations thereof, comprising administering a composition comprising the MRI

detectable species of any one of claims 1 to 5 and imaging the organs, tissues or combinations thereof using nuclear magnetic resonance.

18. (Previously presented) A method of diagnosing tumors in an animal, comprising administering a composition comprising the MRI detectable species of any one of claims 1 to 5 and imaging the animal using nuclear magnetic resonance.

19. (Cancelled)

20. (Currently amended) A process for the preparation of the MRI detectable species of claim 1, said process comprising:

- conjugating the spacer S, if present, with the nutrient or pseudo-nutrient molecule N and combining the obtained conjugated product with the chelating ligand L; or
- conjugating the chelating ligand L with the spacer S, if present, and combining the obtained conjugated product with the nutrient or pseudo-nutrient molecule N; and
- metallating the ~~chelating~~ chelating group L of the obtained conjugated compound with the selected paramagnetic metal ion.